

Musicogenic epilepsy

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A case of musicogenic epilepsy is reported in which the seizures were precipitated by singing voices. It was found that some singers' voices were particularly epileptogenic and that some of their songs, but not others, would precipitate a seizure. A study of the "offending" songs and singers did not reveal a common key, chord, harmonic interval, pitch or rhythm, and the emotional feeling or intensity of the music did not seem to be relevant. However, the voices that caused the seizures had a throaty, "metallic" quality. Such a singing voice results from incorrect positioning of the larynx such that it is not allowed to descend fully during singing; consequently, the vowel sounds produced must be manipulated by the lips or jaw to be distinguished. This trait is most common in singers with a low voice range who sing softly and use a microphone. It is not seen in trained operatic or musical theatre singers. The results of repeated testing showed that the seizures in this patient were caused by listening to singers who positioned the larynx incorrectly.

Présentation d'un cas d'épilepsie musicogène où les crises sont précipitées par la voix chantée. Celle de certains chanteurs est particulièrement épileptogène, mais seuls certains de leurs morceaux le sont. L'analyse de ces voix et des morceaux en cause ne révèle aucun facteur commun dans la tonalité, les accords, les intervalles harmoniques, la hauteur des sons et le rythme; le sentiment du morceau et l'intensité sonore ne comptent pas non plus.

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Mais les voix en cause ont toutes un caractère guttural "métallique" dont on sait qu'il provient de l'attitude vicieuse d'un larynx qui ne descend pas complètement au moment de la phonation, ce qui oblige le chanteur à former ses voyelles par des mouvements du maxillaire inférieur ou des lèvres. C'est le fait de celui dont la voix possède peu d'étendue, qui chante doux dans un microphone. Ce phénomène ne s'observe pas chez les artistes formés au répertoire lyrique. Chez cette malade des essais répétés ont montré que ses crises sont bien provoquées par l'écoute de chanteurs dont le larynx est "mal placé".

Musicogenic epilepsy is one form of reflex or sensory-evoked epilepsy. Critchley¹ noted the following general features of musicogenic epilepsy: the onset is usually during the middle years; music as a precipitating factor is often noticed only after many years of seizures; patients have an above-normal appreciation of music; and the musicogenic factors vary from patient to patient, different musical forms acting as the epileptogenic stimulus.

In the literature there are 73 cases of musicogenic epilepsy, in which varied and often multiple musical stimuli have produced seizures.¹⁻¹⁰ These stimuli include music played on the piano, organ, violin and other string instruments, pure tones, church bells and various forms of music, such as classical, jazz, western and pop. We found six reports of patients who were noted to have seizures induced by music that included singing.²⁻⁷ In this paper we present a unique case of a woman who had a very specific form of musicogenic epilepsy — that is, only the voices of certain singers were the stimuli. We attempted to clarify the basis of the epileptic stimulus in this patient.

Case report

Clinical history and findings

A 53-year-old divorced woman

was seen because her epilepsy seizures were frequent and poorly controlled by medication. Her seizures had begun at age 15 years, and she related their onset to a head injury she had received when a schoolmate pulled a chair out from under her. She had then begun to have frequent falls, staring spells and "funny feelings". She was treated with phenytoin and phenobarbital, but there was only a moderate decrease in the frequency of her seizures.

The seizures occurred 5 to 15 times a month, each lasting from 10 seconds to 3 minutes. A seizure would begin with an epigastric sensation, fear and depersonalization. During the seizure the patient would stare, pull at her clothes, and stand up and walk unsteadily. She would not answer a question but would say Yes repeatedly. She would look bewildered and confused. As the seizure cleared she would feel depressed and have fears of death and senility. Five minutes after the seizure her behaviour and emotional state would be normal.

Twelve years after the onset of the seizures the patient's husband had noticed a relation between many of her seizures and music. The patient later observed that only the voices of certain singers caused the seizures. The seizures were unrelated to the intensity, loudness or pitch of the music but seemed to be due to a unique quality of a singer's voice. Orchestral and instrumental music did not cause seizures. A frequent observer noted that when a seizure occurred during the musical theme of a television show or a commercial message it would not always occur at the same point. Although certain singers' voices were particularly epileptogenic, the seizures did not occur with all of the songs by those artists. The patient usually knew as soon as the singer started to sing that that particular song would cause a seizure. She did not associate this trend with a particular high or low tone, with a difference between male and female singers, or

with emotional factors, such as lyrics of a song. Background singing of which she was not consciously aware also caused seizures. She had had no musical training, but she did have a great appreciation of music and liked many of the singers whose voices caused her seizures.

The patient had no family history of epilepsy. At the time of writing she was taking carbamazepine, 800 mg/d, and primidone, 1000 mg/d. With this and earlier anticonvulsant therapy the frequency of her seizures has decreased. Conditioning with music was effective only for a particular song and did not seem to affect her overall sensitivity to music.

Resting electroencephalogram (EEG) tracings were often normal,

but some showed bilateral synchronous bursts of high-voltage sharp waves, sometimes greater on the left side. The frequency of these waves increased when the singing was heard, and a seizure would occur within seconds to minutes (Fig. 1). Interictal EEGs occasionally showed moderate frontotemporal dysrhythmic activity but were often normal.

Experiment

After studying the music that was epileptogenic in our patient we hypothesized that the causative factor was a particular style of singing in which the mouth rather than the larynx was the primary resonating chamber, since all the singers had audible vocal characteristics of

"mouth singing". This hypothesis allowed us to predict when other singers' voices would cause seizures in our patient.

The patient was subjected in a test laboratory to a variety of music, including vocal recordings and singing by the first author, who had been trained as a singer. In several sessions numerous selections were played during continuous EEG monitoring. The EEG tracings demonstrated the sudden bilateral epileptic activity that occurred within seconds to minutes after the patient heard an "offending" voice. At one session we used a video tape to record the patient's seizure while she was listening to the voice of a popular singer.

We then played three different

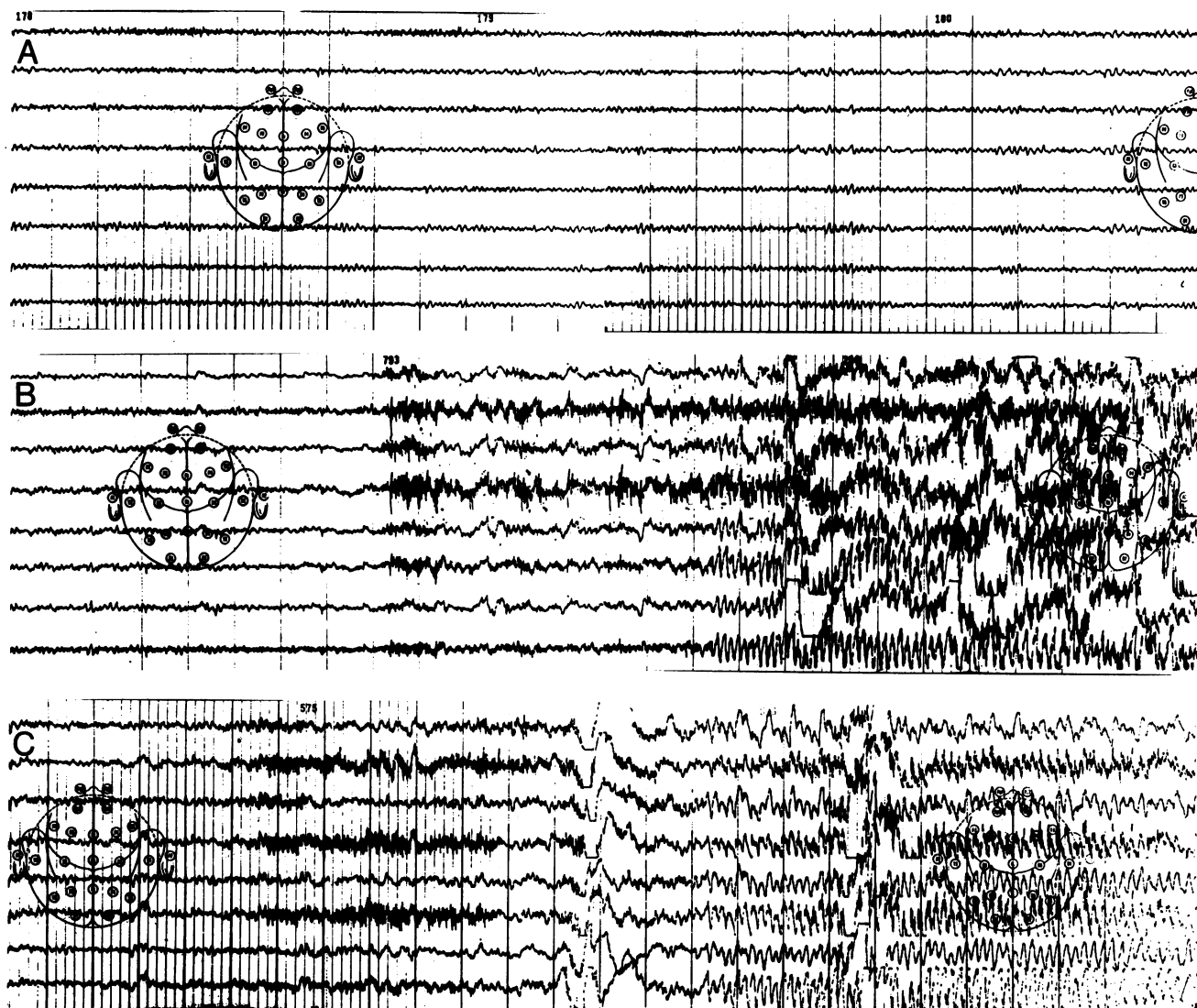


Fig. 1—A: Normal resting electroencephalogram. B: Initiation of seizure 30 seconds after first listening to a recording by Frankie Lane. C: Initiation of seizure 48 seconds after first listening to a recording by Anne Murray. Montage: parasagittals to ipsilateral ear.

sets of music at random: music that had previously caused a seizure, music we predicted would cause a seizure and music we predicted would not cause a seizure. The music in the last two categories consisted of songs that the patient had never heard before.

All the music predicted to cause a seizure did indeed cause an "aura" or a seizure (the music was often stopped as soon as the aura developed or when the EEG showed epileptic bursts). Such music included songs by gospel singer Tennessee Ernie Ford, contemporary singer Dan Hill and folk singer Carole King. The music predicted not to cause seizures did not. This music included choral selections (mainly religious Christmas music), Latin plainsong, orchestral piano music, instrumental organ music and numerous vocal selections from a Broadway musical.

One example demonstrates the specificity of the vocal stimulus in our patient. During the playing of "Tapestry", by Carole King, the patient was restless and said that she would have a seizure if the music was not stopped. Then the first author sang "Tapestry" in a style so different from that of Carole King that the patient only recognized it after one verse. She showed no apprehension and said that she enjoyed the author's singing. Then the author repeated the song, this time imitating Carole King's throaty sound. After three lines of the song the patient had a seizure. The author could consistently cause a seizure within 10 to 15 seconds by "mouth singing" in the manner of certain pop singers and even by singing a cappella (thus eliminating the possibility of a media-produced stimulus — that is, a mechanical factor).

As to why some songs by a particular singer caused seizures and others did not, we noted that some of them were sung softly, with a twang, and others were sung loudly, with greater projection of the voice; the former style more commonly produced a seizure. With repeated playing, the songs were consistent in their tendency to cause or not cause a seizure, and the patient could identify the songs that were a problem.

Discussion

It appears that there are two types of musicogenic epilepsy, one that depends on mechanical factors and one that is evoked by themes, emotions or messages in the music. Critchley¹ suggested that the seizures are caused either by one instrument despite the tune or by one tune despite the instrument. The case we have described exemplifies the former, the instrument being the voice. Our patient had reproducible seizures that were clinically recorded on EEGs and video tape. The unique musical stimulus was found to be an element of the singer's voice.

Careful study of the voices of the singers and of the first author demonstrated no common key, chord, harmonic interval, pitch, volume intensity or rhythm in the songs that provoked seizures. Such general vocal characteristics as tone quality, tonal colour, range, resonance and technical peculiarities were also explored. The common factor among the songs that caused seizures was a throaty sound made by some singers when their singing and articulation were performed by the mouth rather than the throat.

The "open-throat" technique used by trained singers is the result of the increased anterior-posterior, transverse and vertical dimensions of the resonant column of air during speech sounds. Proper positioning of the larynx within the phonatory tube is the main factor in an excellent vocal technique.¹¹ The lowered position of the larynx, which allows for maximum resonance, coupled with articulation, enables the singer to use the voice to portray musical colour (e.g., emotional depth). If either of the antagonistic muscle groups dominates, the length and tension of the larynx become shortened and fixed. Consequently, the singer must depend on only mouth articulation for colour and on technical devices (i.e., a microphone) for amplification.

The resonator of vocal tone in formally trained singers should always be in the pharyngeal cavities, not the mouth, as the resonator must be adjusted, or "tuned", for each vowel and pitch produced. The increased area available for resonance allows the singer to use the

pharyngeal cavities as an "intrinsic microphone".

The first author found that when she made the necessary adjustments to her voice (i.e., singing with a "throaty" quality) the patient had a seizure within 10 to 15 seconds. Conversely, when the author sang with her larynx positioned correctly her "correct" rendition of the same music did not cause a seizure.

The singers with "offending" voices generally have a throaty, "metallic" voice owing to incorrect positioning of the larynx. If the larynx is not allowed to descend freely to produce correct vowel sounds all of the vowel sounds will be similar. The mouth is set rigidly for each vowel, and movement of the lips or jaw modifies the quality. Without the use of the laryngeal cavities as the primary resonating chamber the "mouth singer" portrays musical colour by vowel mutilation. An exaggerated example of this localized sound is the twang in many country and western singers' voices. In this type of singing the pure vowel sound is approximated, and the duration of the phonetically correct vowel sound is minimal. The "epileptic" vowel sounds also alter the intervowel glides (the slurs and swells of intensity on each note) and thus cause the singer's voice to exhibit a pinched vibrato and a slight glissando (i.e., an upward slide to a particular note). Country and western singers, using a diphthong mode of articulation, exemplify the manner in which "microphone" singers manipulate vowel production to enrich their voices with the necessary colour that can be fully achieved only by correct positioning of the larynx. These factors cause impure tones, which are postulated to be the factors precipitating the musicogenic seizures that our patient experienced. The seizures did not occur with operatic or musical theatre soprano singing because of the mandatory projection and the range needed to sing this type of music properly.

Perhaps we should not refer to the pop singer's technique as incorrect since it is an integral part of the sound and the attraction of this genre of music. It is the difference between this technique and that of the trained operatic or musical theatre singer that we want to make clear.

Prescribing Information

Lopresor® (metoprolol tartrate)

50 mg and 100 mg tablets

200 mg slow-release tablets

Therapeutic Classification

Antihypertensive and anti-anginal agent.

Actions

Metoprolol tartrate is a beta-adrenergic-receptor-blocking agent with predominant blocking effect on beta₁ receptors.

Indications

a) Mild and Moderate Hypertension:

Usually used in combination with other drugs, particularly a thiazide diuretic, however, may be tried alone as an initial agent in those patients whose treatment should be started with a beta-blocker rather than a diuretic. The combination of Lopresor with a diuretic or peripheral vasodilator has been found to be compatible and generally more effective than Lopresor alone. Incompatibility with other antihypertensive agents has not been found, experience is limited however. Not recommended for the emergency treatment of hypertensive crises.

b) Angina Pectoris

Lopresor is indicated in patients with angina pectoris due to ischemic heart disease.

Contraindications

Sinus bradycardia, second and third degree A-V block, right ventricular failure secondary to pulmonary hypertension, congestive heart failure, cardiogenic shock, anesthesia with agents that produce myocardial depression, e.g. ether and chloroform.

Warnings

a) **Cardiac Failure:** Special caution should be exercised when administering Lopresor to patients with a history of heart failure, since inhibition with beta-blockade always carries the potential hazard of further depressing myocardial contractility and precipitating cardiac failure. In patients without a history of cardiac failure, continued depression of the myocardium can lead to cardiac failure. At the first sign of impending cardiac failure, patients should be digitalized and/or given a diuretic and observed closely.

Lopresor does not abolish the inotropic action of digitalis on the heart muscle, however, the positive inotropic action of digitalis may be reduced by the negative inotropic effect of Lopresor when the two drugs are used concomitantly. The effects of beta-blockers and digitalis are additive in depressing A-V conduction. If cardiac failure continues, despite adequate digitalization and diuretic therapy, discontinue Lopresor therapy.

b) **Abrupt Cessation of Therapy with Lopresor:** Warn patients against abrupt discontinuation. There have been reports of severe exacerbation of angina, and of myocardial infarction or ventricular arrhythmias in patients with angina following abrupt discontinuation of beta-blocker therapy. The last two complications may occur with or without preceding exacerbation of angina pectoris. When discontinuation of Lopresor is planned in patients with angina, dosage should be gradually reduced over a period of about two weeks and the patient carefully observed. The same frequency of administration should be maintained. In situations of greater urgency, Lopresor should be discontinued stepwise, under conditions of closer observation. If angina markedly worsens or acute coronary insufficiency develops, it is recommended that treatment with Lopresor be reinstituted promptly, at least temporarily.

c) Various skin rashes and conjunctival xerosis have been reported. A severe syndrome (oculo-muco-cutaneous syndrome) whose signs include conjunctivitis sicca and psoriasisiform rashes, otitis, and sclerosing serositis has occurred with the chronic use of one beta-adrenergic-blocking agent (practolol) but has not been observed with Lopresor or any other such agent. Physicians should be alert to the possibility of such reactions and should discontinue treatment in the event that they occur.

d) Severe sinus bradycardia may occur, in such cases, dosage should be reduced.

e) Lopresor may mask the clinical signs of continuing hyperthyroidism or complications and give a false impression of improvement. Therefore, abrupt withdrawal of Lopresor may be followed by an exacerbation of the symptoms of hyperthyroidism including thyroid storm.

Precautions

a) Careful monitoring of patients with diseases associated with bronchospasm is mandatory and a bronchodilator must be administered concomitantly.

b) Administer with caution to patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic blockers may mask the premonitory signs and symptoms of acute hypoglycemia.

c) Adjust dosage individually when used concomitantly with other anti-hypertensive agents.

d) Closely monitor patients also receiving catecholamine-depleting drugs, such as reserpine or guanethidine. Lopresor should not be combined with other beta-blockers.

e) Appropriate laboratory tests should be performed at regular intervals during long-term treatment.

f) Lopresor should not be given to patients receiving verapamil. In exceptional cases, when in the opinion of the physician concomitant use is considered essential, such use should be instituted gradually, in a hospital setting, under careful supervision.

g) **In patients undergoing elective or emergency surgery:** Lopresor should be withdrawn gradually following recommendation given under Abrupt Cessation of Therapy (see WARNINGS). Available evidence suggests that the clinical and pharmacological effects of beta-

blockade induced by Lopresor are no longer present 48 hours after cessation of therapy.

In emergency surgery, effects of Lopresor may be reversed, if necessary, by sufficient doses of such agonists as isoproterenol or levaterenol.

h) **Usage in pregnancy and nursing mothers:** Lopresor crosses the placental barrier and appears in breast milk. It should not be given to pregnant women as it has not been studied in human pregnancy. If use of the drug is deemed essential in nursing mothers, the patient should stop nursing.

i) **Usage in children:** There is no experience with Lopresor in the pediatric age groups.

Adverse reactions

Cardiovascular: Congestive heart failure (see WARNINGS), secondary effects of decreased cardiac output which include: syncope, vertigo, lightheadedness and postural hypotension; severe bradycardia, lengthening of PR interval, second and third degree A-V block, sinus arrest, palpitations, chest pains, cold extremities, Raynaud's phenomenon, claudication, hot flushes.

Central Nervous System: headache, dizziness, insomnia, mental depression, lightheadedness, anxiety, tinnitus, weakness, sedation, vivid dreams, vertigo, paresthesia. **Gastrointestinal:** diarrhea, constipation, flatulence, heartburn, nausea and vomiting, abdominal pain, dryness of mouth.

Respiratory: shortness of breath, wheezing, bronchospasm, status asthmaticus.

Allergic/Dermatological (see WARNINGS): exanthema, sweating, pruritus, psoriasisiform rash.

EENT: blurred vision and non-specific visual disturbances, itching eyes.

Miscellaneous: tiredness, weight gain, decrease in libido.

Clinical Laboratory: The following laboratory parameters have been rarely elevated: transaminases, BUN, alkaline phosphatase and bilirubin. Thrombocytopenia and leucopenia have been reported rarely.

Symptoms and Treatment of Overdosage

Symptoms: bradycardia, congestive heart failure, hypotension, bronchospasm, hypoglycemia.

Treatment: Discontinue Lopresor and observe patient closely. In addition, if required, the following therapeutic measures are suggested.

1. Bradycardia, and hypotension:

Initially 1-2 mg of atropine sulfate should be given intravenously. If a satisfactory effect is not achieved, a pressor agent such as norepinephrine may be administered after preceding treatment with atropine.

2. Heart Block: (second or third degree)

Isoproterenol or transvenous cardiac pacemaker.

3. Congestive heart failure:

Conventional therapy.

4. Bronchospasm:

Aminophylline or a beta₂-agonist.

5. Hypoglycemia:

Intravenous glucose.

Large doses of isoproterenol can be expected to reverse many of the effects of excessive doses of Lopresor.

However, the complications of excess isoproterenol, e.g. hypotension and tachycardia, should not be overlooked.

Dosage and Administration

a) **Hypertension:** Initial Dose: 50 mg b.i.d. If adequate response is not seen after one week, dosage should be increased to 100 mg b.i.d. In some cases the daily dosage may need to be increased by further 100 mg increments at intervals of not less than two weeks up to a maximum of 200 mg b.i.d., which should not be exceeded.

Usual Maintenance Dose: 150-300 mg daily.

When combined with another antihypertensive agent which is already being administered, Lopresor should be added initially at a dose of 50 mg b.i.d. After 1 or 2 weeks the daily dosage may be increased if required, in increments of 100 mg, at intervals of not less than 2 weeks, until adequate blood pressure control is obtained.

b) **Angina pectoris:** Initial Dose: 50 mg b.i.d. for the first week. If response is not adequate, the daily dosage should be increased by 100 mg for the next week. The need for further increases should be closely monitored at weekly intervals and the dosage increased in 100 mg increments to a maximum of 400 mg/day in 2 or 3 divided doses.

Usual Maintenance Dosage: 200 mg/day.

Dosage Range: 100-400 mg per day in divided doses.

A dose of 400 mg/day should not be exceeded.

c) **Slow-release Lopresor SR 200 mg:** Lopresor SR 200 mg

is intended only for maintenance dosing in those patients requiring doses of 200 mg per day.

Treatment must always be initiated and individual titration of dosage carried out using the regular tablets.

Patients with hypertension or angina pectoris on a maintenance regimen of one 100 mg tablet twice daily may be changed to one Lopresor SR 200 mg tablet taken in the morning.

Lopresor SR 200 mg tablets should be swallowed whole.

Availability

Lopresor

Tablet: 50 mg:

Film coated, light red, capsule-shaped tablet, embossed 51 and scored on one side and GEIGY on the other.

Tablet: 100 mg:

Film coated, light blue, capsule-shaped tablet, embossed 71 and scored on one side and GEIGY on the other.

Lopresor SR

Slow-release Tablet: 200 mg:

Film-coated, light yellow, round tablet, embossed GEIGY on one side and CDC on the other.

Product monograph supplied on request.



G-2070

Geigy

Mississauga, Ontario
LSN 2W5

We thank Professor Jefferson Morris, associate professor of voice, Faculty of Music, Dalhousie University, for his advice, and Dr. Andrew Kertesz, University of Western Ontario, for referring his patient. We are especially grateful to our patient for her cooperation during the repeated and prolonged study over the last few years.

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